Claims

1. A method of magnetically manipulating a cell *in vivo* which comprises the association of a magnetisable particle with a cell

2. A method of magnetically manipulating a cell which comprises the association of a magnetisable particle with a cell characterised in that the method comprises agonising or antagonising ion channels within the cell .

3. A method according to claims 1 or 2 characterised in that the method comprises associating the magnetisable particle with an antibody, or an enzyme.

4. A method according to claim 1 or 2 characterised in that particles are associated intracellularly or extracellularly.

5. A method according to claim 4 characterised in that particles are associated intracellularly.

6. A method according to claim 5 characterised in that particles are associated with the N-terminal region of the ion channel.

7. A method according to claim 5 characterised in that particles are associated with the COOH terminal region of the ion channel.

8. A method according to claim 2 characterised in that the method is an *in vivo* method.

9. A method according to claim 2 characterised in that the method is an *ex vivo* method.

10. A method according to claims 1 or 2 characterised in that the particle is a nanoparticle.

11. A method according to claims 1 or 2 characterised in that the method comprises the remote manipulation of a cell.

12. A method according to claims 1 or 2 characterised in that the cell is a mammalian cell.

13. A method according to claims 1 or 2 characterised in that the cell is a bacterial cell.

14. A method according to claims 1 or 2 characterised in that the cell is a plant cell.

15. A method according to claim 11 characterised in that the cell is derived from connective or neuronal tissue.

16. A method according to claim 15 characterised in that the cell is derived from bone, neurons, cardiac cells or any combination thereof.

17. A method according to claim 2 characterised in that the ion channel is a mechanosensitive ion channel.

18. A method according to claim 17 characterised in that the mechanosensitive ion channel has been transfected into a cell.

19. A method according to claims 17 or 18 characterised in that the ion channel is a voltage-gated ion channel.

20. A method according to claims 17 or 18 characterised in that the ion channel is a ligand-gated ion channel.

21. A method according to claim 2 characterised in that the ion channel is selected from the group a including sodium channel, potassium channel, calcium channel, chloride channel and a non-selective cation channel or any combination thereof.

22. A method according to claim 21 characterised in that the ion channel is selected from a calcium or a potassium ion channel.

23. A method according to claim 22 characterised in that the ion channel is a potassium ion channel.

24. A method according to claim 23 characterised in that the potassium channel is a TREK-1 channel.

25. A method of manipulating a mechanosensitive ion channel characterised in that the method comprises the association of a magnetisable particle with an ion channel.

26. A method according to claim 1, 2 or 25 characterised in that the magnetisable material is selected from the group which includes elemental iron (Fe), or a compound thereof, and a chromium compound, or a combination thereof.

27. A method according to claim 26 characterised in that the iron compound is an iron salt.

28. A method according to claim 27 characterised in that the iron salt is selected from the group which includes magnetite (Fe_3O_4), maghemite (γFe_2O_3) and greigite (Fe_3S_4), or any combination thereof.

29. A method according to claim 26 characterised in that the chromium compound is a chromium salt.

30. A method according to claim 29 characterised in that the chromium salt is chromium oxide (CrO_2).

31. A method according to claim 1, 2 or 25 characterised in that the magnetic material comprises particles which comprises a magnetic core with a biocompatible coating.

32. A method according to claim 31 characterised in that the particle has a core and a silica shell enveloping the core.

33. A method according to claim 32 characterised in that the particle is selected from those comprising (a) a core comprising a magnetisable particle and (b) a silica shell enveloping the core.

34. A method according to claim 33 characterised in that the magnetisable particle is selected from the group, which includes elemental iron (Fe), or a salt thereof and a chromium salt, or a combination thereof.

35. A method according to claim 25 characterised in that the particle is a porous particle with multiple magnetic centre within the pores.

36. A method according to claim 1, 2 or 25 characterised in that the particles have a mean size of 5000 nm or less.

37. A method according to claim 36 characterised in that the particles have a mean size of from 1 nm to 5000 nm.

38. A method according to claim 1, 2 or 25 characterised in that the method comprises the application of a remote magnetic field on the magnetisable particles.

39. A method according to claim 1, 2 or 25 characterised in that the particle is tagged with one or more specific antibodies or protein binding motifs which recognise key cellular elements within a cell.

40. A method according to claim 37 characterised in that the specific antibodies or protein binding motifs are selected from transmembrane extracellular matrix molecules, adhesion molecules or dispersed membrane adhesion proteins or extracellular matrix proteins.

41. A method according to claim 40 characterised in that the method is *in vivo*.

42. A method according to claim 40 characterised in that the specific antibodies or protein binding motifs are transmembrane adhesion or extracellular matrix molecules.

43. A method according to claim 42 characterised in that the transmembrane adhesion molecules are selected from integrins, cadherins, selectins, and immunoglobulins.

44. A method according to claim 41 characterised in that the specific antibodies or protein binding motifs are selected from dispersed membrane adhesion proteins.

45. A method according to claim 44 characterised in that the dispersed membrane adhesion protein is RGD (arginine-glycine-aspartate).

46. A method of treatment of a patient suffering from a disorder in which an ion channel plays a role which comprises the administration to such a patient of

magnetisable particles as hereinbefore described and manipulating the ion channels or cells using a magnetic field external to the body.

47. A method of destroying cells or inhibiting cell growth which comprises agonising or antagonising ion channels within a cell by the association of a magnetisable particle with a cell.

48. A method of inducing osmotic shock to a cell which comprises agonising or antagonising ion channels within a cell by the association of a magnetisable particle with a cell.

49. A method of treatment or alleviation of a tumour cell which comprises a method according to claim 46.

50. A method according to claim 49 characterised in that the tumour cell is a cancer cell.

51. A method of treatment of a patient according to claim 47 characterised in that the method comprises the killing of cells via holding ion channels open with a targeted static magnetic field.

52. A method of treatment of a patient according to claim 47 characterised in that the method comprises the killing of cells via cyclically opening and closing ion channels with a targeted, time-varying magnetic field.

53. A method of treatment according to claim 47 in which a disorder may involve a number of tissues in the body where ion channels play a key role in normal cellular homeostasis.

54. A method according to claim 53 characterised in the cells are cardiac muscle cells.

55. A method according to claim 53 characterised in that the method comprises the treatment of hypertension.

56. A method according to claim 53 characterised in that the method comprises pain relief.

57. A method according to claim 56 characterised in that the method comprises anaesthesia.

58. A method according to claim 57 characterised in that the anaesthesia is localised.

59. A method of treatment of a patient according to claim 46 characterised in that the method comprises tissue and/or bone repair.

60. A method of treatment according to claim 59 characterised in that the cells are selected from ligamentum cells, tenocytes, chondrocytes and other stromal cells (such as chondrocyte progenitor cells).

61. A method of treatment according to claim 59 characterised in that the method comprises the regeneration of tissue or the generation of artificial tissue, such as skin, cartilage, ligament, tendon, muscle or bone.

62. A method of treatment according to claim 59 characterised in that the method comprises the remote activation of ion channels.

63. A method of treatment according to claim 59 characterised in that the method comprises wound healing and/or tissue adhesion.

64. A method of treatment according to claim 59 characterised in that the method comprises bone repair and/or bone growth.

65. A method of treatment according to claim 46 characterised in that the method comprises a dental or veterinary application.

66. A method for establishing localised anaesthesia through the action of ion channel modulation by a magnetic field external to the body.

67. A method according to claim 66 characterised in that the pain relief comprises anaesthesia.

68. A method of treatment according to claim 46 characterised in that the method comprises the use of a magnetic field at a frequency of from 0.1 to 10 Hz.

69. A method of treatment according to claim 46 characterised in that the method comprises the use of a magnetic field will typically have a flux density of from 10 mT to 1400 mT.

70. A method of inducing a therapeutic effect in a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell and magnetically manipulating the magnetisable particle.

71. A method of treatment which comprises the administration of a therapeutically active agent which may be administered simultaneously, separately or sequentially with a magnetisable particle whilst agonising or antagonising ion channels within the cell.

72. A method of targeting a therapeutically active agent to a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell, magnetically manipulating the magnetisable

particle and simultaneously, separately or sequentially administering the therapeutically active agent.

73. The use of a magnetisable particle in a method of magnetically manipulating a cell *in vivo* wherein the method comprises the association of a magnetisable particle with a cell.

74. The use of a magnetisable particle in the manufacture of a system for magnetically manipulating a cell which system comprises the association of a magnetisable particle with a cell and agonising or antagonising ion channels within the cell.

75. The use according to claims 73 or 74 characterised in that the method comprises associating the magnetisable particle with an antibody, or an enzyme.

76. The use according to claim 73 or 74 characterised in that particles are associated intracellularly or extracellularly.

77. The use according to claim 76 characterised in that particles are associated intracellularly.

78. The use according to claim 77 characterised in that particles are associated with the N-terminal region of the ion channel.

79. The use according to claim 77 characterised in that particles are associated with the COOH terminal region of the ion channel.

80. The use according to claim 74 characterised in that the method is an *in vivo* method.

81. The use according to claim 74 characterised in that the method is an *ex vivo* method.

82. The use according to claims 73 or 74 characterised in that the particle is a nanoparticle.

83. The use according to claims 73 or 74 characterised in that the method comprises the remote manipulation of a cell.

84. The use according to claims 73 or 74 characterised in that the cell is a mammalian cell.

85. The use according to claims 73 or 74 characterised in that the cell is a bacterial cell.

86. The use according to claims 73 or 74 characterised in that the cell is a plant cell.

87. The use according to claim 83 characterised in that the cell is derived from connective or neuronal tissue.

88. The use according to claim 87 characterised in that the cell is derived from bone, neurons, cardiac cells or any combination thereof.

89. The use according to claim 74 characterised in that the ion channel is a mechanosensitive ion channel.

90. The use according to claim 89 characterised in that the mechanosensitive ion channel has been transfected into a cell.

91. The use according to claims 89 or 90 characterised in that the ion channel is a voltage-gated ion channel.

92. The use according to claims 66 or 67 characterised in that the ion channel is a ligand-gated ion channel.

93. The use according to claim 74 characterised in that the ion channel is selected from the group a including sodium channel, potassium channel, calcium channel, chloride channel and a non-selective cation channel or any combination thereof.

94. The use according to claim 93 characterised in that the ion channel is selected from a calcium or a potassium ion channel.

95. The use according to claim 94 characterised in that the ion channel is a potassium ion channel.

96. The use according to claim 94 characterised in that the potassium channel is a TREK-1 channel.

97. The use of a magnetisable particle in the manufacture of a system for use in a method of manipulating a mechanosensitive ion channel characterised in that the method comprises the association of a magnetisable particle with an ion channel.

98. The use according to claim 73, 74 or 97 characterised in that the magnetisable material is selected from the group, which includes elemental iron (Fe), or a compound thereof and a chromium compound, or a combination thereof.

99. The use according to claim 98 characterised in that the iron compound is an iron salt.

100. The use according to claim 100 characterised in that the iron salt is selected from the group, which includes magnetite (Fe_3O_4), maghemite (γFe_2O_3) and greigite (Fe_3S_4), or any combination thereof.

101. The use according to claim 98 characterised in that the chromium compound is a chromium salt.

102. The use according to claim 101 characterised in that the chromium salt is chromium oxide (CrO_2).

103. The use according to claim 73, 74 or 97 characterised in that the magnetisable material comprises particles which comprise a magnetic core with a biocompatible coating.

104. The use according to claim 103 characterised in that the particle has a core and a silica shell enveloping the core.

105. The use according to claim 104 characterised in that the particle is selected from those comprising (a) a core comprising a magnetisable particle and (b) a silica shell enveloping the core.

106. The use according to claim 105 characterised in that the magnetisable particle is selected from the group, which includes elemental iron (Fe), or a salt thereof and a chromium salt, or a combination thereof.

107. The use of a magnetisable particle in the manufacture of a system for inducing a therapeutic effect in a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell and magnetically manipulating the magnetisable particle.

108. The use according to claim 107 characterised in that a therapeutically active agent is administered simultaneously, separately or sequentially with agonising or antagonising ion channels within the cell.

109. The use of a magnetisable particle in the manufacture of a system for targeting a therapeutically active agent to a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell, magnetically manipulating the magnetisable particle and simultaneously, separately or sequentially administering the therapeutically active agent.

110. The use according to claim 97 characterised in that the particle is a porous particle with multiple magnetic centre within the pores.

111. The use according to claim 73, 74 or 97 characterised in that the particles have a mean size of 5000 nm or less.

112. The use according to claim 110 characterised in that the particles have a mean size of from 1 nm to 5000 nm.

113. The use according to claim 73, 84 or 97 characterised in that the method comprises the application of a remote magnetic field on the magnetisable particles.

114. The use according to claim 73, 74 or 97 characterised in that the particle is tagged with one or more specific antibodies or protein binding motifs which recognise key cellular elements within a cell.

115. The use according to claim 114 characterised in that the specific antibodies or protein binding motifs are selected from transmembrane extracellular matrix molecules, adhesion molecules or dispersed membrane adhesion proteins or extracellular matrix proteins.

116. The use according to claim 115 characterised in that the method is *in vivo*.

117. The use according to claim 115 characterised in that the specific antibodies or protein binding motifs are transmembrane adhesion or extracellular matrix molecules.

118. The use according to claim 117 characterised in that the transmembrane adhesion molecules are selected from integrins, cadherins, selectins, and immunoglobulins.

119. The use according to claim 116 characterised in that the specific antibodies or protein binding motifs are selected from dispersed membrane adhesion proteins.

120. The use according to claim 119 characterised in that the dispersed membrane adhesion protein is RGD (arginine-glycine-aspartate).

121. The use of a magnetisable particle in the manufacture of a system for the treatment of a patient suffering from a disorder in which an ion channel plays a role which comprises the administration to such a patient of magnetisable particles as hereinbefore described and manipulating the ion channels or cells using a magnetic field external to the body.

122. The use of a magnetisable particle in the manufacture of a system for destroying cells or inhibiting cell growth which comprises agonising or antagonising ion channels within a cell by the association of a magnetisable particle with a cell.

123. The use of a magnetisable particle in the manufacture of a system for inducing osmotic shock to a cell which comprises agonising or antagonising ion channels within a cell by the association of a magnetisable particle with a cell.

124. The use of a magnetisable particle in the manufacture of a system for the treatment or alleviation of a tumour cell which comprises a method according to claim 49.

125. The use according to claim 124 characterised in that the tumour cell is a cancer cell.

126. The use according to claim 122 characterised in that the method comprises the killing of cells via holding ion channels open with a targeted static magnetic field.

127. The use according to claim 122 characterised in that the method comprises the killing of cells via cyclically opening and closing ion channels with a targeted, time-varying magnetic field.

128. The use according to claim 121 in which a disorder may involve a number of tissues in the body where ion channels play a key role in normal cellular homeostasis.

129. The use according to claim 128 characterised in the cells are cardiac muscle cells.

130. The use according to claim 128 characterised in that the use comprises the manufacture of a system for the treatment of hypertension.

131. The use according to claim 128 characterised in that the use comprises the manufacture of a system for the treatment of pain relief.

132. The use according to claim 131 characterised in that the use comprises the manufacture of a system for the treatment of anaesthesia.

133. The use according to claim 132 characterised in that the anaesthesia is localised.

134. The use according to claim 121 characterised in that the use comprises the manufacture of a system for tissue and/or bone repair.

135. The use of treatment according to claim 134 characterised in that the cells are selected from ligamentum cells, tenocytes, chondrocytes and other stromal cells (such as chondrocyte progenitor cells).

136. The use according to claim 134 characterised in that the use comprises the manufacture of a system for the regeneration of tissue or the generation of artificial tissue, such as skin, cartilage, ligament, tendon, muscle or bone.

137. The use according to claim 134 characterised in that the system utilises remote activation of ion channels.

138. The use according to claim 134 characterised in that the use comprises the manufacture of a system for wound healing and/or tissue adhesion.

139. The use according to claim 134 characterised in that the use comprises the manufacture of a system for bone repair and/or bone growth.

140. The use according to claim 121 characterised in that the use comprises the manufacture of a system for dental or veterinary application.

141. The use of a magnetisable particle in the manufacture of a system for establishing localised anaesthesia through the action of ion channel modulation by a magnetic field external to the body.

142. The use according to claim 141 characterised in that the pain relief comprises anaesthesia.

143. The use according to claim 121 characterised in that the method comprises the use of a magnetic field at a frequency of from 0.1 to 10 Hz.

144. The use according to claim 121 characterised in that the method comprises the use of a magnetic field will typically have a flux density of from 10 mT to 1400 mT.

145. The use according to claim 116 characterised in that the use comprises manipulating cells from outside the body.

146. The use according to claim 116 characterised in that the use comprises a method of tissue repair and/or bone repair.

147. The use according to claim 116 characterised in that the use comprises a method of pain relief.

148. The use according to claim 147 characterised in that the pain relief comprises anaesthesia.

149. The use of a magnetisable particle in the manufacture of a system for inducing a therapeutic effect in a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell and magnetically manipulating the magnetisable particle.

150. The use of a magnetisable particle in the manufacture of a system comprising a therapeutically active agent which may be administered simultaneously, separately or sequentially with the magnetisable particle whilst agonising or antagonising ion channels within the cell.

151. The use of a magnetisable particle in the manufacture of a system for targeting a therapeutically active agent to a cell which comprises agonising or

antagonising ion channels within the cell by the association of a magnetisable particle with the cell, magnetically manipulating the magnetisable particle and simultaneously, separately or sequentially administering the therapeutically active agent.

152. A kit comprising a therapeutically active agent and means for associating a magnetisable particle with a cell.

153. A method or use substantially as described with reference to the accompanying drawings.